iPSC-Derived Human Microglia-like Cells to Study Neurological Diseases.

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Public Summary:
Microglia play critical roles in brain development, homeostasis, and neurological disorders. Here, we report that human microglial-like cells (iMGLs) can be differentiated from iPSCs to study their function in neurological diseases, like Alzheimer's disease (AD). We find that iMGLs develop in vitro similarly to microglia in vivo, and whole-transcriptome analysis demonstrates that they are highly similar to cultured adult and fetal human microglia. Functional assessment of iMGLs reveals that they secrete cytokines in response to inflammatory stimuli, migrate and undergo calcium transients, and robustly phagocytose CNS substrates. iMGLs were used to examine the effects of Abeta fibrils and brain-derived tau oligomers on AD-related gene expression and to interrogate mechanisms involved in synaptic pruning. Furthermore, iMGLs transplanted into transgenic mice and human brain organoids resemble microglia in vivo. Together, these findings demonstrate that iMGLs can be used to study microglial function, providing important new insight into human neurological disease.

Scientific Abstract:
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